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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/930,715	08/14/2001	Moncef Jendoubi	266/226	1686

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EXAMINER	
TRAN, MY CHAU T	

ART UNIT	PAPER NUMBER
1639	14

DATE MAILED: 11/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/930,715	JENDOUBI, MONCEF	
	Examiner	Art Unit	
	My-Chau T. Tran	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-23* is/are rejected.

7)☒ Claim(s) *15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/28/03 has been entered.

2. Applicant's amendment filed 8/28/03 in Paper No. 13 is acknowledged and entered. Claims 1-13 are canceled by the amendment. Claims 14-23 are added by the amendment.

3. Claims 14-23 are pending.

Claim Objections

4. Claim 15 is objected to as an improper dependent claim since it depends on cancel claim 1 that result in a broken pendency chain. However in order to further prosecution, Claim 15 is interpreted to depend on claim 14. Appropriate correction is required.

5. Claims 14-23 are treated on the merit in this Office Action.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 22 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of an antibody (polyclonal or monoclonal) in making a matrix of protein array (pg. 10, lines 15-21; pg. 13, lines 10-24; pg. 16, lines 3-6) and to conduct gene product expression profiling of a given normal or diseased tissue (pg. 6, lines 7-15; pg. 19, lines 23-27; pg. 20, lines 3-8), does not reasonably provide enablement for the scope encompassed by the claim. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with this claim that is to raise a monoclonal antibody to the expression product of the gene sequence.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re* Wands USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

It is noted that there is a great deal of unpredictability in raising a monoclonal antibody to the expression product of the gene sequence without knowing specifically the sequence to be use for making the antibody. The method for raising a monoclonal antibody requires different method steps (i.e. different reagents) from the method of analyzing differential gene expression of Claim 14. The instant specification fails to provide a specific methodological procedure for which the instant method can or is intended to be used for raising a monoclonal antibody to the expression product of the gene sequence. The specification teachings are directed to the methods for making a matrix of protein array and conducting gene product expression profiling of a given normal or diseased tissue (e.g. analyzing differential gene expression).

The working examples in the specification are limited to the methods for making a matrix of protein array, and conducting gene product expression profiling of a given normal or diseased tissue. Such is not seen as sufficient to support the breath of the claims, wherein the scope of the claims encompasses the method of raising a monoclonal antibody to the expression product of the gene sequence. It is noted that the Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves, see *In re* Gardner et al. 166 USPQ 138 (CCPA 1970). Therefore, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

It is noted that this rejection was previously made for claim 12 in the office action mailed on 10/18/02 wherein applicant overcome the rejection by canceling of claim 12.

8. Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (This is a written description rejection).

The present claim is drawn to a method of raising a monoclonal antibody to the expression product of the gene sequence.

The specification discloses the use of an antibody (polyclonal or monoclonal) in making a matrix of protein array (pg. 10, lines 15-21; pg. 13, lines 10-24; pg. 16, lines 3-6) and to conduct gene product expression profiling of a given normal or diseased tissue (pg. 6, lines 7-15; pg. 19, lines 23-27; pg. 20, lines 3-8). None of these meet the written description provision of 35 U.S.C 112, first paragraph. The specification provides insufficient written description to support the method encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* ,

> 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, the full breadth of the claim does not meet the written description provision of 35 U.S.C 112, first paragraph.

In the presence instance, the claim contains no specific sequence or method steps regarding the method of raising a monoclonal antibody to the expression product of the gene sequence. The specification does not provide sufficient written description to support the method encompassed by the claim.

It is noted that this rejection was previously made for claim 12 in the office action mailed on 10/18/02 wherein applicant overcome the rejection by canceling of claim 12.

9. Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (This is a written description rejection).

The present claim is drawn to a method of determining the polynucleotide sequence of the gene sequence.

The specification discloses only the use of a matrix protein array for the analysis of gene product (pg. 6, lines 16-22; Example 3 and 4). None of this meets the written description

provision of 35 U.S.C 112, first paragraph. The specification provides insufficient written description to support the method encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, the full breadth of the claim does not meet the written description provision of 35 U.S.C 112, first paragraph.

In the presence instance, the claim contains no method steps regarding the method of determining the polynucleotide sequence of the gene sequence. The specification does not provide sufficient written description to support the method encompassed by the claim.

It is noted that this rejection was previously made for claim 13 in the office action mailed on 10/18/02 wherein applicant overcome the rejection by canceling of claim 13.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 16, and 22-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Clarification is needed for the limitation of "*containing the proteins in discrete areas of an array that physically separate the at least two samples*" in claim 14, because it is unclear as to it correlation with the method step of providing at least two samples (e.g. the areas of the array "contains" the proteins of the two samples or the two samples themselves). It is suggested that if the areas of the array contains the proteins of the two samples the term "providing" should replace the term "containing").

b. The term "gene sequence" of Claim 14, 15, and 21 is vague and indefinite because no specific sequence is provided by the claim or the specification.

c. The phrase "comprised performed" of claim 16 is vague and indefinite because it is unclear as to the limitation of the contacting step of the at least two samples. Additionally, it is unclear as to the relationship between the two samples and the 100 samples (e.g. how can one start with two samples and end up with 100).

d. The correlation of the method step of claim 21 and the method of claim 14 is vague and indefinite because the first step of the method of differential gene expression is providing the expression product (protein) of the gene sequence (e.g. the expression product is known). Additionally, the method step of claim 21 is a contradiction to the identifying step of claim 14.

e. The method of determining the polynucleotide sequence of the gene sequence of Claim 23 is vague and indefinite because it is not clear how it is related with the method of analyzing differential gene expression of Claim 14. The method of determining the polynucleotide sequence of the gene sequence would involve different method steps that have different functions and effects than the method steps for analyzing differential gene expression. It is noted that this rejection was previously made for claim 13 in the office action mailed on 10/18/02 wherein applicant overcome the rejection by canceling of claim 13.

12. Claim 14-23 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the "signaling" element for the detection of the antibody binding.

13. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: The method step of providing the type of host animal to be

use for raising the antibody or the cell lines use for culturing the antibody. The method step of adding adjuvants to increase the immunological response of host animal. It is noted that this rejection was previously made for claim 12 in the office action mailed on 10/18/02 wherein applicant overcome the rejection by canceling of claim 12.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

15. Claims 14-15, and 17-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Iris et al. (US Patent 6,403,309 B1; *filing date of 3/19/1999*).

Iris et al. discloses a method for the analysis of gene expression using addressable antibody array (col. 14, lines 51-67). The method is used to directly monitor qualitative and quantitative gene expression levels in tissue biopsies or histological preparations that is taken from patient with suspected genetic disorder. The sample is from a human (col. 6, lines 58-65). The solid phase surface comprises a plurality of loci, wherein each locus comprises an antibody specific to one or more of the peptides of the peptide label oligonucleotide probes (col. 6, lines 28-31; col. 22, lines 23-29). The antibodies includes polyclonal or monoclonal (refers to instant claim 2) (col. 23, lines 33-57). The polyclonal antibodies are produce from mice or rat. The detection of a signal would indicate the present of the target (col. 16, lines 12-19). The method of Iris et al. anticipated the method of the claimed invention.

Response to Arguments

16. Applicant's argument(s) directed to the above rejection under 35 USC 102(e) as being anticipated by Iris et al. (US Patent 6,403,309 B1) for claims 1-11 (***e.g. new claims 14-21***) were considered but they are not persuasive for the following reasons.

Applicant contends that the method of Iris et al. does not anticipate the presently claimed invention because the method of Iris et al. does not disclose that the "[r]eaction between an antibody that is specific for the expression product of a gene and a protein present in the patient sample such that differentially expressed genes are identified".

Applicant's arguments are not convincing since the method of Iris et al. does anticipate the presently claimed method. The method of Iris et al. disclosed that the antibodies have

specific affinity to the peptide-linked oligonucleotide probes (e.g. antibody reaction with the protein) (col. 22, lines 27-29). And the method of Iris et al. is not only for the detection or measurement of the level of an alternatively spliced or mis-spliced RNA in a tissue sample, but also for directly monitoring qualitative and quantitative gene expression levels in a tissue sample (e.g. identifying the differentially expressed genes from the reaction of the antibody to the protein) (col. 14, lines 56-61). Therefore, the method of Iris et al. does anticipate the presently claimed method.

17. Claims 14-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Bandaru (US Patent 6,462,187 B1; *filing date of 6/15/2000*).

Bandaru discloses a method of comparing the level of expressed polypeptide before and after treatment of the disorder (e.g. biological conditions) (col. 4, lines 9-13). The disorder includes cancerous condition (col. 10, lines 21-55). The method of detection comprised of detecting the binding interaction of the antibody specific to the expressed polypeptide (col. 37, lines 36-47). The method comprise of a two dimensional array having a plurality of addresses, each address of the plurality is positionally distinguishable from each other address of the plurality (col. 4, lines 35-45; col. 51, lines 37-67). Each address of the plurality can have a unique capture probe such as polypeptide, e.g. an antibody specific for the polypeptide. The plurality of addresses includes at least 10, 100, 500, 1,000, 5,000, 10,000, 50,000 addresses (col. 49, lines 14-16). The array can be use to assay gene expression in a tissue to ascertain tissue specificity of genes in the array (col. 49, lines 62-64) or to monitor expression of one or more genes in an array with respect to time for ascertaining differential expression patterns of one or

more genes in normal or abnormal cells (col. 50, lines 32-45). Therefore the method of Bandaru anticipated the presently claimed method.

18. Claims 14-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Wagner et al. (US Patent 6,329,209 B1; *filing date 7/14/1999*).

Wagner et al. disclosed a method of comparing the protein expression of two cells or a population of cells that have been exposed to different conditions (col. 37, lines 19-67). The method comprises an array of protein-capture agents arranged in discrete, known regions of patches (col. 9, lines 66-67 to col. 10, lines 1-12). The array can have any number of a plurality of different protein-capture agents (col. 11, lines 1-11). For instance, an array comprise of about 10,000 patches would comprise of about 10,000 different protein-capture agents (col. 11, lines 28-33). Therefore, the number of different protein-capture agents on an array will vary depending on the application desired (col. 11, lines 12-13). The protein-capture agent would include biomolecule such as protein or polynucleotide (col. 4, lines 48-67) and would binds specifically to the antibody of interest (col. 12, lines 48-52). Therefore the method of Wagner et al. anticipates the presently claimed method.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 703-305-6999. The examiner can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 703-306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

mct
November 14, 2003

PADMASHRI PONNALURI
PRIMARY EXAMINER